AF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Lee Mizzen *et al.*	Art Unit	: 1645
Serial No.	: 09/001,737	Examiner	: S. Devi
Filed	: December 31, 1997		
Title	: STREPTOCOCCAL HEAT SHOCK PROTEINS OF THE HSP60 FAMILY		

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL

Appellants are appealing the final rejection of claims 2, 3, 5-7, 19-24, 31 and 38-45 in the Office action dated June 9, 2004 (herein, "the Office action"). A Notice of Appeal was filed on October 12, 2004, and received by the U.S. Patent and Trademark Office on October 14, 2004. A Petition for an extension of time is being filed herewith.

(1) Real Party in Interest

The real party in interest is Stressgen Biotechnologies Corporation, having a place of business at #350 - 4243 Glanford Avenue, Victoria, BC, Canada V8Z 4B9.

(2) Related Appeals and Interferences

There are no prior or pending appeals, interferences, or judicial proceedings related to the present application.

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(3) Status of Claims

According to the Summary of the Office action, with which Appellants disagree:

claims 2, 3, 5-7, 19-24, 31, 35, and 38 are **pending**;

claims 4, 8, 32, and 34 are **withdrawn** from consideration;

claims 2, 3, 5-7, 19-24, 31, and 38-45 are **rejected**; and

claims 33 and 35 are **objected to**.

For the reasons given below, Appellants contend that claims 2-8, 19-24, 31-35 and 38-45 are **pending**. The Examiner's list of pending claims fails to include the claims withdrawn from consideration as well as some of the rejected claims (claims 39-45) and one of the claims objected to (claim 33). In the prior Office action, mailed June 6, 2003, the Summary indicated that claims 1-39 were pending. Appellants then **canceled** claims 1, 9-18, 25-30, and 36-37 and added new claims 40-45. Thus, claims 2-8, 19-24, 31-35, and 38-45 must be pending. This is in agreement with the Examiner's statement on page 2 of the Office action ("[c]laims 2-8, 19-24, 31-35, and 38-45 are pending").

(4) Status of Amendments

All of the amendments in this case have been entered.

(5) Summary of Claimed Subject Matter

The present invention features compositions related to the bacterium *Streptococcus pyogenes*, which is the causative agent associated with acute pharyngitis ("strep throat"), acute rheumatic fever, impetigo, and toxic shock-like syndrome. The compositions include isolated nucleic acid molecules; vectors and other compositions that include the isolated nucleic acids; and host cells that include the vectors. More specifically, **independent claim 2** covers an isolated nucleic acid molecule encoding a *Streptococcus pyogenes* Hsp60 (*see* the specification at page 1, lines 4-7). **Independent claim 3** covers an isolated nucleic acid molecule that includes the sequence of SEQ ID NO:5 from nucleotides 15-1649, the sequence of SEQ ID NO:7 from nucleotides 15-1652, or sequences complementary thereto (*see* the specification at page 5, lines 13-21). **Independent claim 4** covers an isolated nucleic acid molecule that includes at least 24 nucleotides and that hybridizes to SEQ ID NO:5 from nucleotides 15-1649 or a sequence

complementary thereto under particularly stated stringency conditions (*see* the specification at page 5, lines 13-23, particularly lines 21-23, and page 31, line 27 through page 32, line 1). **Independent claim 5** covers an isolated nucleic acid molecule that includes a nucleotide sequence that is identical to a segment comprising at least 25% of the contiguous nucleotide bases of SEQ ID NO:5 from nucleotides 15-1649, of SEQ ID NO:7 from nucleotides 15-1652, or of a sequence complementary thereto (*see* the specification at page 5, line 28 through page 6, line 3). **Independent claim 6** covers an isolated nucleic acid molecule that includes a nucleic acid sequence that encodes a polypeptide having a sequence that is at least 95% homologous to SEQ ID NO:6 or SEQ ID NO:8 (*see* the specification at page 6, lines 3-6). **Independent claim 8** covers an isolated nucleic acid molecule that includes a nucleotide sequence that encodes a polypeptide that includes at least eight contiguous amino acids from amino acids 1-544 of SEQ ID NO:6 (*see* the specification at page 6, lines 11-16). **Independent claim 41** covers isolated nucleic acid molecules consisting of 12, 14-18 or 24 nucleotides that hybridize to SEQ ID NO:7 from nucleotides 15-1652 or a complement thereof under specified conditions of stringency (*see* the specification at page 32, lines 9-14, and page 12, lines 24-29). The **dependent claims** cover, *inter alia*, vectors that include the isolated nucleic acid molecules of any of claims 2-8 (*see* the specification at page 7, lines 18-23 and page 11, lines 5-8) and host cells (*see* the specification at page 7, lines 23-26, and page 15, line 28 through page 23, line 5).

(6) Grounds of Rejection

Claims 5, 6, 19-24, 31, 38 and 39 are rejected under 35 U.S.C. § 112, ¶ 1, as lacking an adequate written description.

Claims 7, 19-24, 31 and 41-45 are rejected under 35 U.S.C. § 112, ¶ 2, as indefinite.

Claims 3, 5, 19-24, 31 and 40-45 are rejected under 35 U.S.C. § 102(e), as anticipated by Kunsch *et al.* (U.S. Patent No. 6,420,135).

Claim 2 is rejected under 35 U.S.C. § 102(b), as anticipated by Hamel *et al.* (WO 96/40928).

Claims 3 and 40 are rejected under 35 U.S.C. § 102(b), as anticipated by Probeski (GenEmbl Accession No. X89236, submitted 06/29/95).

(7) Argument

The Specification Adequately Describes the Subject Matter Claimed

Claims 5, 6, 19-24, 31, 38 and 39 stand rejected under 35 U.S.C. § 112, ¶ 1. The Examiner states, "[t]his is a written description rejection" (Office action dated June 6, 2003, at page 6).

The Written Description Guidelines (Federal Register, vol. 66, no. 4, Notices pp. 1099-1111, 05 January 2001) were referenced frequently in the prosecution history. While those Guidelines are also referenced below, Appellants recognize that they do not have the force and effect of law. Thus, relevant court decisions regarding the statutory requirement for an adequate written description are provided, and it is in accordance with those decisions that the present ground for rejection should be withdrawn.

An Applicant's specification should clearly convey that he or she invented the claimed subject matter. *In re Barker*, 559 F.2d 588 (CCPA 1977). The specification must put the public in possession of that subject matter. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), *cert. denied* 523 U.S. 1089 (1998). It is that – the conveyance of the invention to the public – that is given in exchange for the right to exclude others from practicing the invention for the duration of the patent's term. *Eldred v. Ashcroft*, 537 U.S. 186 (2003).

An adequate description is one that describes the claimed invention in sufficient detail that one of ordinary skill in the art can reasonably conclude that the inventor had possession of the claimed invention. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991). Possession may be shown in a variety of ways. For example, possession can be found where an Applicant presents drawings of the claimed invention (as in *Vas-Cath*) or structural chemical formulas. An Applicant may also describe distinguishing identifying characteristics. *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55 (1998); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200 (Fed. Cir. 1991) (one may define a compound by "whatever characteristics sufficiently distinguish it").

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by: actual reduction to practice; reduction to drawings; or disclosure of relevant identifying characteristics. MPEP at 2163(3)(a)(ii), citing *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997). A "representative number of species" means that the species that are adequately

described are representative of the entire genus. MPEP at 2163(3)(a)(ii), citing *Enzo Biochem.*, 323 F.3d at 966, 63 USPQ2d at 1615 and *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004).

The Examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. MPEP at 2163(II)(A), citing *Wertheim*, 541 F.2d 257 (CCPA 1976).

In the present case, the Examiner has argued that Appellants have failed to provide a representative number of the nucleic acid molecules claimed and to establish a nexus between the structure and function of the claimed nucleic acid molecules.

With respect to the number of species disclosed, the Examiner stated, "[t]he specification ... does not indicate what distinguishing attributes are shared by the members of the genus" (Office action dated April 10, 2001, at page 4). The Examiner's language echoes a portion of the *Written Description Guidelines* from the January 2001 *Federal Register* (at page 1106; emphasis added):

> Satisfactory disclosure of a "representative number" [of species] depends on whether one of skill in the art would recognize that the applicant was in possession of the *necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.*

In contrast to the Examiner's assertion, Appellants have made it very clear what attributes the claimed nucleic acid molecules have in common, and one of ordinary skill in the art would surely recognize those attributes. It is clear from the plain language of the claims that all of the nucleic acid molecules must include a certain sequence. For example, the nucleic acid molecules of claim 5 must all include a sequence that is identical to at least 25% of the contiguous nucleotides of SEQ ID NO:7 from nucleotides 15-1652, *and such sequences are explicitly described in the specification* (*see, e.g.*, page 5, line 28 through page 6, line 3). Thus, Appellants described, in their specification, a specific sequence (that represented by nucleotides 15-1652 of SEQ ID NO:7) and variants thereof (nucleic acids that contain at least 25% of the contiguous

nucleotides of SEQ ID NO:7 from nucleotide 15 to nucleotide 1652). Only a simple mathematical exercise is required to determine how many nucleotides constitute at least 25% of the referenced sequence.

By way of illustration, a person of ordinary skill in the art, upon reading Appellants' specification, would find: (a) SEQ ID NO:7 and (b) the statement that "the present invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that is identical to a segment comprising at least 25% of contiguous nucleotide bases of ... SEQ ID NO:7 from nucleotides 15-1652" (specification at page 5, line 28, through page 6, line 3). Could that person then reasonably conclude that Appellants possessed nucleotides 15-1652 of SEQ ID NO:7? Yes, as the Examiner acknowledges (Office action dated June 9, 2004, at page 6). Could that person also reasonably conclude that Appellants possessed a nucleic acid containing nucleotides 15-1000 of SEQ ID NO:7? Yes, as that nucleic acid would contain at least 25% of the referenced sequence. Could that person also reasonably conclude that Appellants possessed a nucleic acid containing only nucleotides 15-300 of SEQ ID NO:7? No, because that nucleic acid would not contain at least 25% of the specified bases within SEQ ID NO:7. Obviously, many other nucleic acids could be used in this illustration, and it would be just as readily apparent to one of ordinary skill in the art whether Appellants possessed those sequences or not.

By describing SEQ ID NO:7 and by specifying a particular portion of SEQ ID NO:7 (the portion defined by the "at least 25%" limitation), Appellants have described the necessary common attributes of *all* of the nucleic acid molecules claimed (molecules having sequences in addition to those of SEQ ID NO:7 and homologues of SEQ ID NO:7 are discussed further below). Writing out one exemplary sequence after another would add nothing more. It is apparent from their description that Appellants were in possession of the claimed sequences, many though they be. The nucleic acid molecules were quite clearly described in the specification and quite clearly recited in Appellants' claims. Given Appellants' description, one of ordinary skill in the art would have no difficulty in perceiving the sequences described and in concluding that Appellants were in possession of those sequences.

The Examiner disagrees, stating that "irrespective of the simplicity of the method of isolation (or simplicity of the math involved in counting off the nucleotides)," "one of skill in the art cannot envision the detailed chemical structure of the encompassed nucleic acid

molecules ... absent precise description" (Office action dated June 9, 2004, at page 6). According to the Examiner, a sufficiently precise description requires substantial testing. The Examiner stated that "[t]he precise structure ... of each DNA molecule ... can only be determined empirically by *actually making every DNA molecule* that encodes the polypeptide" (Office action dated June 6, 2003 at page 6; emphasis added). Appellants have argued that there is absolutely no requirement that they actually make every molecule that falls within the scope of their claims and, in the most recent Office action (dated June 9, 2004), the Examiner appeared to agree. Still, the Examiner argued that Appellants must "demonstrate success" with "a representative number" of the nucleic acid molecules claimed (the Office action at page 6). This, too, is contrary to the law. While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity. *Fiers v. Ravel*, 984 F.2d 1164, 1169 (Fed. Cir. 1993). Appellants have described the nucleic acid molecules they now claim *with particularity*. That is, in such a way that one of ordinary skill in the art could conclude that Appellants possessed those molecules. For written description, nothing more is required.

The Examiner's insistence on evidence of success seems to emerge from a belief that Appellants must describe "the essential structural features of the claimed nucleic acid molecules" and/or establish "a correlation between a particular structure and function" (the Office action at page 7). This remark is made amidst numerous statements regarding Appellants' failure to demonstrate that the nucleic acid molecules they claim are functional (the Office action at pages 6-10). For example, the Examiner states (at page 8; emphasis added):

> Other than ... SEQ ID NO:7 ..., the structure of a representative number of *functional* (i.e., *S. pyogenes*-specific) nucleic acid variant or segment species that are currently encompassed within the claimed genus is not adequately described.

The Examiner also refers to the Written Description Guidelines as stating:

> There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function (the Office action at page 10).

For the record, the first sentence quoted by the Examiner does not appear in the Guidelines. The nearest statement Appellants can find reads (at page 1105, right-hand column), "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of the disclosure necessary to satisfy the written description requirement." Furthermore, that sentence is not followed by the second sentence shown above ("[f]or example, ..."). Instead, the second sentence shown above is a part of footnote 49 (although imprecisely quoted). Significantly, footnote 49 annotates the section of the Guidelines that instructs Examiners how to assess the adequacy of the description when the specification contains only an *incomplete* structure. That section reads (page 1106, middle-column; emphasis added):

> *[if]* the application as filed does not disclose the complete structure ... of the claimed invention as a whole, [*then* an Examiner should] determine whether the specification discloses *other relevant identifying characteristics* sufficient to describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention.

Thus, an Examiner should only look for an established correlation between structure and function when Applicants provide an incomplete structure. This is made explicitly clear in the remainder of footnote 49:

> Thus, the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function.

Here, Appellants have more than "minimal structure." Indeed, they have provided the complete sequence of SEQ ID NO:7 and have described the particular and readily identifiable variants that constitute the invention they claim.

Not surprisingly, the Guidelines are consistent with the case law regarding the sufficiency of the written description. In the instant case, the Examiner has referenced and quoted *Fiers v. Ravel*, 984 F.2d 1164, 1170 (Fed. Cir. 1993) ("[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is the DNA itself") (the Office action at page 10). The Examiner's continued reliance on *Fiers* is not understood. The Federal Circuit found that one of

the specifications at issue in *Fiers* – that belonging to Ravel – lacked an adequate written description *because Ravel did not provide the sequence of the DNA he attempted to claim.* The facts of *Fiers*, with respect to Ravel, are contrary to the facts of the instant case, where Appellants **do** disclose the sequence of the DNA they wish to claim. Moreover, in *Fiers*, the Federal Circuit also considered a specification belonging to Sugano. The court concluded "that Sugano's application satisfies the written description requirement since it sets forth the complete and correct nucleotide sequence of a DNA coding for β-IF and thus 'convey[s] with reasonable clarity to those skilled in the art that, as of the filing date sought, [Sugano] was in possession of the [DNA coding for β-IF.]'" *Fiers* at 1172. The instant facts are much closer to those surrounding Sugano's application than they are to those surrounding Ravel's. Here, as with Sugano, the specification describes the structure of the nucleic acid claimed (including specified residues of SEQ ID NO:7 and, with particularity, portions thereof). Here, as with Sugano, there is an adequate written description.

The Examiner has also cited *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991) ("Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred") (the Office action at page 10). As in *Fiers*, the claims in *Amgen* covered a DNA sequence (*e.g.*, claim 2 covered "[a] purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin [EPO]"). However, the *actual* sequence was not described in the specification. It was in *that* context that the Federal Circuit found conception had not occurred. As there was, therefore, no "definite and permanent idea of the complete and operative invention," the invention could not have been adequately described. The court stated (at 1206; emphasis added):

> *[U]ntil* Fritsch had a complete mental conception of a purified and isolated DNA sequence encoding EPO and a method for its preparation, in which *the precise identity of the sequence is envisioned*, or in terms of other characteristics sufficient to distinguish it from other genes, all he had was an objective to make an invention which he *could not then adequately describe.*

Thus, both *Fiers* and *Amgen* stand for the proposition that, absent structural information, the claiming of a gene, by mere function -- where there is "simply a wish" to know its identity -- does not satisfy the written description requirement. Actual reduction to practice is required

when conception is otherwise incomplete. As noted, the instant facts are significantly different. Appellants' specification does not merely recite the name of a gene or a desired function, but instead describes the *specific nucleic acid sequences* encompassed by the claims. Appellants have reduced their invention to practice and have provided a thoroughly adequate written description.

The forgoing remarks have focused on pending claim 5, but the analysis and conclusion would be the same for claims 6, 38 and 39. These claims cover isolated nucleic acid molecules that include a sequence that encodes a polypeptide that is at least 95%, 97%, or 98% homologous, respectively, to SEQ ID NO:8. The sequence of the polypeptide designated SEQ ID NO:8 is, of course, presented in the specification, and Appellants clearly state that their invention provides "a variant of Hsp60 that is at least 95% homologous to a polypeptide ... of SEQ ID NO:8" (specification at page 6, lines 5-6; *see also* the paragraph bridging pages 11-12, where Appellants specify that the homology may also be greater than 97% or 98%). This description would allow those of ordinary skill in the art, who routinely compare one nucleic acid molecule to another or one polypeptide to another, to conclude that Appellants were in possession of these variants. By describing SEQ ID NO:8 and by specifying that a variant sequence must remain at least 95%, 97%, or 98% homologous to that reference, Appellants have described the necessary common attributes of all of the nucleic acid molecules claimed in claim 6. By reference to a minimum homology, Appellants adequately described not only a representative number of species, but the entire genus of nucleic acids, as one of ordinary skill in the art could immediately vary the sequence in any given way and determine whether the requisite level of homology was retained. There was no need to exemplify sequence after sequence.

The remaining claims rejected on this ground are claims 19-24 and 31. The compositions covered by these claims are described in the specification at, for example, page 7, lines 18-29; page 11, lines 5-15; and page 15, line 28, through page 23, line 5. Various sequences, vectors, and cells are also used throughout the Examples presented on pages 37-49. The Examiner has made no specific comments regarding the adequacy of Appellants' disclosure of these compositions, and Appellants contend that one of ordinary skill in the art would readily conclude that Appellants were in possession of them.

The Examiner has, however, commented on "the open claim language of the claims" (the Office action at page 7). Specifically, the Examiner states that "the open claim language of the claims means that primer pairs outside the sequence of SEQ ID NO:7 from nucleotides 15-1652 are encompassed by the instant claims" (the Office action at pages 7-8). Appellants wish to make it clear that the claims cover portions of SEQ ID NO:7, homologues of SEQ ID NO:7 and, due to the "open" claim language, nucleic acid molecules including at least one additional nucleotide at either end of those defined portions or homologues. However, all of these nucleic acids must still include the sequence specified by the claims and described in the specification; they must still have the common attributes Appellants so fully described when they described the sequence by virtue of its minimal content ("at least 25% of ..." or "at least 95% homologous to..."). The open claim language does broaden the scope of the claims, but it does not broaden it beyond the scope of Appellants' description.

<u>One of Ordinary Skill in the Art Would Understand the Metes and Bounds of the Claims</u>

Claims 7, 19-24, 31 and 41-45 stand rejected under 35 U.S.C. § 112, ¶ 2, as indefinite "for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention" (the Office action at pages 11-12).

Claim 7: Claim 7 covers "[t]he isolated nucleic acid molecule of claim 3, encoding a polypeptide that is selectively bound by an antibody specific for a *Streptococcus pyogenes* Hsp60". In rejecting claim 7, the Examiner states:

> [c]laim 7, as amended, is vague in the recitation: 'encoding a polypeptide that is selectively bound by an antibody specific for a Streptococcus pyogenes Hsp60', because it is unclear how a nucleic acid can encode a polypeptide bound by an antibody (the Office action at page 12).

Appellants fail to see how one of ordinary skill in the art, upon reading claim 7, would be confused as to the metes and bounds of the claim. The Examiner seems to read the claim as requiring that the claimed isolated nucleic acid encode a polypeptide that is *already bound* by an antibody. However, it is quite clear that the phrase "is selectively bound by an antibody" is a functional limitation of the encoded polypeptide. Claim 7 requires a nucleic acid molecule that

encodes a polypeptide, which itself can then be selectively bound by an antibody. As such, claim 7 is not vague, and this ground for rejection should be withdrawn.

Claim 41: Claim 41 covers an isolated nucleic acid molecule consisting of 12, 14-18 or 24 nucleotides that hybridize to a particular sequence (part of SEQ ID NO:7) under specified conditions. The Examiner rejects claim 41, stating:

> A nucleic acid molecule "consisting of" nucleotides (contiguous or discontiguous) is a double-stranded molecule and therefore, it is unclear how such a double-stranded nucleic acid molecule can hybridize to SEQ ID NO:7 from nucleotides 15-1652, which is also double-stranded (the Office action at page 12).

The recitation of a "nucleic acid molecule" does not limit the scope of claim 41 to double stranded molecules (nor does it limit SEQ ID NO:7, recited therein, to that form). Moreover, it is a fundamental concept in molecular biology that hybridization occurs between sense and antisense strands; it is that concept that underlies the double helix. One of ordinary skill in the art would surely be familiar with that concept and, given the language of claim 41, would understand that the claim covers *both* sense and antisense strands of nucleic acid molecules that meet the limitations of the claim. That is, one of ordinary skill in the art would understand that claim 41 covers sequences that hybridize to SEQ ID NO:7 within the region spanning nucleotides 15-1652 *and, as the claim specifies*, sequences that hybridize to a *complement* of SEQ ID NO:7 within the region spanning nucleotides 15-1652 under the conditions specified in the claim. As the metes and bounds of claim 41 are clear, Appellants respectfully request that this rejection be reversed.

Claims 19-24, 31 and 42-45: Claims 19-24 and 31 are rejected because they depend from rejected claim 7, and claims 42-45 are rejected because they depend from rejected claim 41. As the grounds for rejection of claims 7 and 41 have been addressed, Appellants request that the rejection of dependent claims 19-24, 31 and 42-45 also be reversed.

The Claimed Subject Matter is New

There are three separate grounds for rejection based on an alleged lack of novelty. In the first, the Examiner rejects claims 3, 5, 19-24, 31 and 40-45 under 35 U.S.C. § 102(e) as

anticipated by U.S. Patent No. 6,420,135 (herein, "Kunsch"). According to the Examiner (the Office action at page 12; emphasis added):

> the *complementary nucleotide sequence claimed* in claim 3(c) and claims 5 and 40(c) *does not have a size limit*, and therefore encompasses nucleotide sequences that are both partially and fully complementary to the recited nucleic acid molecule.

The Examiner further states that Kunsch teaches a nucleotide sequence "that consist of 17 or 18 bases that are 100% structurally identical with fragments of the instantly recited SEQ ID NO:7" (the Office action at page 13). Thus, the Examiner concludes that the Kunsch sequence would "serve as a complementary sequence to the nucleotide sequence of SEQ ID NO:7 in the region from nucleotides 15 to 1652" (the Office action at page 13). Appellants respectfully disagree.

Claim 3 recites, in relevant part:

> (c) an isolated nucleic acid molecule comprising a sequence complementary to ... the sequence of SEQ ID NO:7 from nucleotides 15-1652.

Claims 5 and 40 include similar limitations; claim 40 is similar to claim 3 except the transitional phrase in claim 40 is "consisting of" rather than "comprising", and claim 5 is similar to claim 3 except the nucleic acid molecule need only include "at least 25%" of the specified reference sequence (a complement of SEQ ID NO: 7 from nucleotides 15-l652).

In each of claims 3, 5, and 40, the claim language specifies that the required complementary sequence is complementary to, or includes a sequence that is complementary to, at least 25% of a reference sequence *from* nucleotides 15-1652 of SEQ ID NO:7. *From* is an inclusive term; the complementary sequence must extend *from* the first specified nucleotide *to* the last. Thus, there *is* a limitation on the size of the claimed nucleic acid molecule. Complementary nucleic acid molecules covered by claims 3 and 40 must include a sequence that is complementary to the *entire recited portion* of SEQ ID NO:7, which is 1638 nucleotides long. Complementary nucleic acid molecules covered by claim 5 must include a sequence that is complementary to at least 409 contiguous nucleotides of the reference sequence (*i.e.*, 25% of SEQ ID NO:7 *from* nucleotides 15-1652).

In order for a prior art reference to anticipate the claimed subject matter, the reference must teach all the limitations of the claims. As Kunsch teaches a nucleotide sequence that, at

most, includes 18 contiguous nucleotides that are complementary to SEQ ID NO:7, Kunsch cannot anticipate the present claims; the present claims require much longer stretches of complementary nucleotides. As such, Appellants respectfully request that the rejection be reversed.

Claims 3 and 40: The Examiner also (and newly) rejected claims 3 and 40 under 35 U.S.C. § 102(b) as anticipated by Podbielski (GenEmbl Accession No. X89236). According to the Examiner:

> Probeski [*sic.*] taught an isolated groEL gene of the heat shock protein 60 of S. pyogenes having more than 86% sequence identity with the instantly recited nucleotide sequence of SEQ ID NO:7 from nucleotides 15-1652 and 100% local sequence identity with long contiguous stretches of the instantly recited nucleotide sequence of SEQ ID NO:7 from nucleotides 15-1652. The prior art nucleotide sequence therefore comprises or serves as a sequence that is complementary to the instantly claimed nucleotide sequence (the Office action at page 13).

Appellants respectfully disagree. As shown by the sequence alignment provided by the Examiner, the longest stretch of contiguous nucleotides taught by Podbielski, which is identical to SEQ ID NO:7, is 263 nucleotides. This stretch spans, in the query ("Qy") sequence, nucleotides 1300-1562. For the reasons provided above, claims 3 and 40 require nucleic acids that include much longer stretches of nucleotides (*i.e.*, 1638 nucleotides). As such, Podbielski cannot anticipate either claim 3 or claim 40.

Claim 2: Claim 2 stands rejected under 35 U.S.C. § 102(b) as anticipated by WO 96/40928 ("Hamel"). Claim 2 covers "an isolated nucleic acid molecule encoding a *Streptococcus pyogenes* Hsp60." Hamel discloses an Hsp70 (*see* Hamel's SEQ ID NOs: 19 and 20). According to the Examiner (the Office action at page 11):

> In view of the lack of structure, i.e., SEQ ID number, for the recited Hsp60 in the claim, the prior art Hsp [*i.e.*, Hsp70] is deemed to meet the claim limitations. The limitation 'Hsp60' is viewed merely as a different name given to the prior art product and does not impart any structure or function that distinguishes the product of the prior art from the claimed product.

Appellants respectfully disagree. Although the Examiner considers Hsp60 and Hsp70 to *differ only in name*, one of ordinary skill in the art would immediately recognize Hsp60 and Hsp70

(and nucleic acids encoding them) as distinct from one another (as evidenced by, for example, the review article Appellants previously submitted (Parsell and Lindquist, *Annu. Rev. Genet.* 27:437-496, 1993)). "Hsp60" is known to differ from "Hsp70", and this is true regardless of Appellants' reference to variants and fragments of Hsp60 in their specification. Those variants and fragments are obviously variants and fragments *of Hsp60*. The recitation of "Hsp60" is an affirmative limitation of claim 2, and the inclusion of variants and fragments *of Hsp60* does not extend the scope of the claim to cover molecules encoding Hsp70. During patent examination, the pending claims must be given their broadest *reasonable* interpretation consistent with the specification. *In re Hyatt*, 211 F.3d 1367 (Fed. Cir. 2000). However, the broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165 F.3d 1359 (Fed. Cir. 1999). It is simply not reasonable to interpret "Hsp60" in a way that completely vitiates its meaning; one of ordinary skill in the art would not do so. Accordingly, Hamel cannot anticipate claim 2, and Appellants respectfully request that this rejection be reversed.

In Accordance with the Office's Policy, the Examiner Should Examine SEQ ID NO:5

Claims 2-8, 19-24, 31-35 and 38-45 are pending. The Examiner has maintained that various claims are withdrawn from consideration because they include non-elected subject matter. Appellants respectfully disagree, contending that the "non-elected subject matter" referred to by the Examiner is patentable subject matter within a single elected invention.

In the Restriction Requirement mailed September 15, 2000, the Examiner required the election of one of four independent inventions:

I. Claims 1, 3-10, 19-24 and 31, drawn to DNA encoding a ***S. pneumoniae*** Hsp60 molecule;

II. Claims 2-10, 19-24 and 31, drawn to DNA encoding a ***S. pyogenes*** Hsp60 molecule;

III. Claims 11-18 and 25-28, drawn to a Hsp60 polypeptide; and

IV. Claims 29-30, drawn to a method of eliciting an immune response.

The Examiner also stated that "[u]pon the election of Group I, II, III, or IV, Applicant's [*sic.*] are *further restricted* to one of the following sequences: SEQ ID NO:1, 2, 3, 4, 5, 6, 7, or 8" (Restriction Requirement at page 2; emphasis added).

In the Response to the Restriction Requirement, Appellants elected the invention of *Group II* "and the *species* of SEQ ID NO:7", which was "embodied by claims 2-5, 7, 10, 19-24 and 31" (Response filed January 16, 2001, at page 1; emphasis added).

In subsequent Office actions, the Examiner indicated that varying claims were withdrawn from consideration. In the most recent Office action (mailed June 9, 2004), the Summary indicates that claims 4, 8, 32, and 34 were withdrawn, while also stating (at page 2; emphasis added):

> [c]laims 3(a); a part of 3(c); claim 4; a part of claims 5 and 6; claim 8; claims 32 and 34; a part of claims 38 and 39; claim 40(a); and a part of 40(c), and claims dependent therefrom or corresponding parts of such dependent claims *are withdrawn from consideration* as being directed to the 'further restricted' and the non-elected nucleic acid molecule of SEQ ID NO:5. See 37 C.F.R. 1.142(b) and M.P.E.P. § 821.03.

Thus, the Examiner maintains that claims that recite SEQ ID NO:5 (*e.g.*, claims 4 and 8) as well as parts of claims that recite SEQ ID NO:5 (*e.g.*, paragraph (c) of claim 3), *which were present in the application as originally filed and within elected Group II*, are directed to non-elected subject matter and are thus withdrawn from consideration. Subsequently added claims, which are also clearly within Group II (*e.g.*, claims 32 and 34) are also withdrawn.

Appellants respectfully request examination of all the subject matter within elected Group II. The published policy of the U.S. Patent and Trademark Office is to examine a reasonable number of nucleotide sequences in a given application. The MPEP at § 2434 states (emphasis added):

> the Commissioner has partially waived the requirements of 37 CFR 1.141 and *will permit* a reasonable number of [independent and distinct] nucleotide sequences to be claimed in a single application. Under this policy, in most cases, *up to 10 independent and distinct nucleotide sequences will be examined in a single application without restriction.*

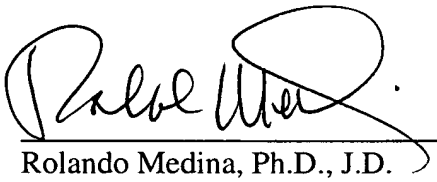
In accordance with this policy, Appellants urge the examination of two sequences: those represented by sequence identifiers 5 and 7. "Where the rights of individuals are affected, it is incumbent upon agencies to follow their own procedures." *Morton v. Ruiz*, 94 S.Ct. 1055 (1974).

In the event the Examiner continues to refuse to examine the claims with respect to SEQ ID NO:5, Appellants respectfully ask for recognition that at least claim 2 is a linking claim and, therefore, when claim 2 (or any other linking claim) is in condition for allowance, SEQ ID NO:5 will be examined.

CONCLUSION

For the reasons set forth above, Appellants respectfully request that the rejection of claims 2, 3, 5-7, 19-24, 31 and 38-45 be reversed and that the claims within Group II be examined with respect to SEQ ID NO:5. The brief fee of $340 is enclosed. Filed herewith is a Petition for Extension of time along with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,



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Appendix of Claims

2. An isolated nucleic acid molecule encoding a *Streptococcus pyogenes* Hsp60.

3. An isolated nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 5 from nucleotides 15-1649;

(b) an isolated nucleic acid molecule comprising the sequence of SEQ ID NO: 7 from nucleotides 15-1652; and

(c) an isolated nucleic acid molecule comprising a sequence complementary to the sequence of SEQ ID NO:5 from nucleotides 15-1649 or complementary to the sequence of SEQ ID NO:7 from nucleotides 15-1652.

4. An isolated nucleic acid molecule comprising at least 24 nucleotides that hybridizes to SEQ ID NO: 5 from nucleotides 15-1649 or to a complement of SEQ ID NO: 5 from nucleotides 15-1649 when hybridization is carried out at 65°C in 6x SSC, 1x Denhardt's solution, and 0.1% SDS, and washing is carried out at 65°C in 0.2x SSC, 1x Denhardt's solution, and 0.1% SDS.

5. An isolated nucleic acid molecule comprising a nucleotide sequence that is identical to a segment comprising at least 25% of contiguous nucleotide bases of SEQ ID NO: 5 from nucleotides 15-1649, SEQ ID NO: 7 from nucleotides 15-1652, a complement of SEQ ID NO: 5 from nucleotides 15-1649, or a complement of SEQ ID NO: 7 from nucleotides 15-1652.

6. An isolated nucleic acid molecule comprising a nucleic acid sequence that encodes a polypeptide comprising a sequence that is at least 95% homologous to SEQ ID NO:6 or SEQ ID NO:8.

7. The isolated nucleic acid molecule of claim 3, encoding a polypeptide that is selectively bound by an antibody specific for a *Streptococcus pyogenes* Hsp60.

8. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising a Streptococcal Hsp60 peptide consisting of at least 8 contiguous amino acids selected from amino acid residues 1-544 of SEQ ID NO: 6, wherein the Streptococcal Hsp60 peptide binds to a major histocompatibility complex molecule.

19. A vector comprising the isolated nucleic acid molecule of any one of claims 2-8.

20. The vector of claim 19, wherein the vector is an expression vector comprising a promoter operatively linked to the isolated nucleic acid molecule.

21. The vector of claim 20, further comprising a selectable or identifiable marker.

22. The vector of claim 20, wherein the promoter is a constitutive or an inducible promoter.

23. A host cell containing the vector of claim 19.

24. The host cell of claim 23, wherein the host cell is selected from the group consisting of a bacterial cell, a mammalian cell, a yeast cell and an insect cell.

31. A composition comprising the isolated nucleic acid molecule of any one of claims 2-8 and a pharmaceutically acceptable carrier or diluent.

32. The nucleic acid molecule of claim 3, wherein the nucleic acid molecule comprises nucleotides 15-1649 of SEQ ID NO:5.

33. The nucleic acid molecule of claim 3, wherein the nucleic acid molecule comprises nucleotides 15-1652 of SEQ ID NO:7.

34. The nucleic acid molecule of claim 6, wherein the polypeptide comprises SEQ ID NO:6.

35. The nucleic acid molecule of claim 6, wherein the polypeptide comprises SEQ ID NO:8.

38. The nucleic acid molecule of claim 6, wherein the polypeptide comprises an amino acid sequence that is at least 97% homologous to SEQ ID NO:6 or SEQ ID NO:8.

39. The nucleic acid molecule of claim 6, wherein the polypeptide comprises an amino acid sequence that is at least 98% homologous to SEQ ID NO:6 or SEQ ID NO:8.

40. The isolated nucleic acid molecule of claim 3, selected from the group consisting of:

(a) an isolated nucleic acid molecule consisting of the sequence of SEQ ID NO: 5 from nucleotides 15-1649;

(b) an isolated nucleic acid molecule consisting of the sequence of SEQ ID NO: 7 from nucleotides 15-1652; and

(c) an isolated nucleic acid molecule consisting of a sequence complementary to the sequence of SEQ ID NO:5 from nucleotides 15-1649 or complementary to the sequence of SEQ ID NO:7 from nucleotides 15-1652.

41. An isolated nucleic acid molecule consisting of 12, 14-18, or 24 nucleotides that hybridizes to SEQ ID NO:7 from nucleotides 15-1652 or to a complement of SEQ ID NO:7 from nucleotides 15-1652 when hybridization is carried out at 65°C in 6x SSC, 1x Denhardt's solution, and 0.1% SDS, and washing is carried out at 65°C in 0.2x SSC, 1x Denhardt's solution, and 0.1% SDS.

42. A vector comprising the isolated nucleic acid molecule of claim 41.

43. The vector of claim 42, wherein the vector is an expression vector comprising a promoter operatively linked to the isolated nucleic acid molecule.

44. A host cell comprising the vector of claim 43.

45. A composition comprising the isolated nucleic acid molecule of claim 41 and a pharmaceutically acceptable carrier or diluent.